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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,589	01/15/2004	Keizo Koya	3211.1001-001	5403

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EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/758,589	KOYA ET AL.	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2008 and 06 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34,35 and 51-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-35 and 51-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Applicants' response and amendments to the claims, filed 10/6/2008, are acknowledged and entered. Claims 8-14, 16, 17, 25-31, 33, and 37-50 have been cancelled by Applicant. Claims 51-57 are newly added. Claims 34-35 and 51-57 are pending and under examination.

Response to Arguments

Any previous rejections and/or objections to claims 8-14, 16, 17, 25-31, 33, and 37-50 are withdrawn as being moot in light of Applicant's cancellation of the claims.

The rejections set forth in the present Office Action constitute the entire set of rejections against the now pending claims.

Terminal Disclaimer

Receipt is acknowledged of the Terminal Disclaimer filed 10/6/2008. The Terminal Disclaimer has been approved and entered.

Claim Rejections - 35 USC § 112 – 2nd Paragraph – New Ground of Rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35 and 56-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims recite a method "comprising" administering to a subject a compound represented by the structural formula recited in the claims. As such, the claims allow for the additional administration of paclitaxel or a paclitaxel analog, or any other additional anticancer agent. However, the claims further recite the limitation, "...wherein the subject is *optionally* co-administered an effective amount of a second anti-cancer agent *other than* paclitaxel or a paclitaxel analog". The metes and bounds of the claims are unclear because it is not apparent whether the optional co-administration of a second

anti-cancer agent other than paclitaxel or a paclitaxel analog precludes the co-administration of paclitaxel or a paclitaxel analog that is encompassed by the recited "comprising" language. In other words, one interpretation of the claims is that the recited compound can be co-administered with paclitaxel or a paclitaxel analog or optionally co-administered with a second anti-cancer agent *other than* paclitaxel or a paclitaxel analog. Alternatively, one could interpret the claims to mean that the administration of paclitaxel or a paclitaxel analogue is excluded from the "comprising" language of the claims. In order to clarify the intended meaning of the claims, the Examiner suggests removing the "optionally co-administered" language and inserting therefore, "...wherein when the subject is co-administered an effective amount of a second anti-cancer agent, the second anti-cancer agent is not paclitaxel or a paclitaxel analog".

Claim Rejections - 35 USC § 102 – New Ground of Rejection

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 57 is rejected under 35 U.S.C. 102(e) as being anticipated by **Koya *et al.*** (US 2003/0119914 A1; Published Jun. 26, 2003; Filed Jul. 10, 2002).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Koya *et al.* teach methods of treating a subject with cancer comprising administering a compound of Formula (I) in combination with taxol or an analog of taxol. The reference thus anticipates an embodiment of claim 57 wherein the claimed compound is administered with a

second anti-cancer agent that is paclitaxel or an analog of paclitaxel (see 35 U.S.C. 112, 2nd Paragraph rejection discussed *supra*). The claimed compound is a compound encompassed by the methods of Koya *et al.* and is explicitly recited as a preferred compound of the invention (page 1, Compound (1); Example 12). Melanoma as recited in claim 57 is explicitly taught as a cancer treatable with the methods taught in Koya *et al.* (page 7, [0077]).

Accordingly, Koya *et al.* anticipate the claimed method of treating melanoma wherein Compound (1) is administered in combination with paclitaxel or an analogue of paclitaxel. As discussed *supra*, one interpretation of the claim is that the recited compound is administered with a second anti-cancer agent that could be paclitaxel or an analog of paclitaxel and an alternate, optional embodiment encompasses administration of a second active agent that is not paclitaxel or an analog of paclitaxel.

Claim Rejections - 35 USC § 103 – New Ground of Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 34-35 and 51-57 are rejected under 35 U.S.C. 103(a) as being obvious over **Koya *et al.*** (US 2003/0119914 A1; Published Jun. 26, 2003; Filed Jul. 10, 2002) in view **Everitt *et al.*** (US 2002/0198160 A1; Published Dec. 26, 2002; Filed Apr. 29, 2002).

The applied reference (Koya *et al.*) has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Koya *et al.* teach methods of treating a subject with cancer comprising administering a compound of Formula (I) in combination with taxol or an analog of taxol. The claimed compound is a compound encompassed by the methods of Koya *et al.* and is explicitly recited as a preferred compound of the invention (page 1, Compound (1); Example 12). Melanoma as recited in claim 57 is explicitly taught as a cancer treatable with the methods taught in Koya *et al.* (page 7, [0077]). Koya *et al.* additionally teach that "sarcoma" is a cancer that may be treated using the disclosed methods.

Koya *et al.* differ from claims 34-35, 52 and 54 in that the reference does not disclose the treatment of "multi-drug resistant" cancers. Koya *et al.* differ from claim 56 in that the reference does not disclose the treatment of uterine sarcoma.

However, Everitt *et al.* teach methods of enhancing the bioavailability of pharmaceutically active agents comprising co-administering with the active agent lopinavir (Abstract; page 1, [0008]). Lopinavir is disclosed to inhibit P-glycoprotein, which is found in cancerous tumor cells and enhances multi-drug resistance (page 1, [0006]). Accordingly, Everitt *et al.* disclose methods for treating multi-drug resistance comprising co-administering a pharmaceutically active agent to treat the multi-drug resistance and lopinavir (page 2, [0013]). With respect to the treatment of cancer, Everitt *et al.* discloses the use of taxanes such as

paclitaxel as preferable active agents to be used in conjunction with lopinavir (page 5, [0043]). The inventors demonstrate that lopinavir inhibits P-glycoprotein's ability to efflux paclitaxel, thereby increasing paclitaxel's potency, even in cells that show resistance to treatment with paclitaxel alone (page 5, [0045]). Cancers disclosed to be treatable with the methods disclosed in Everitt include melanomas, leukemias, and uterine tumors (page 2, [0021]).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have administered the claimed compound in combination with paclitaxel or an analog of paclitaxel and lopinavir for the treatment of melanoma, leukemia, uterine sarcoma, multi-drug resistant uterine sarcoma, multi-drug resistant leukemia, or multi-drug resistant melanoma. While Koya *et al.* do not explicitly teach the treatment of multi-drug resistant cancers, Everitt *et al.* disclose methods of overcoming multi-drug resistance comprising administering paclitaxel in combination with lopinavir. As such, one skilled in the art at the time the invention was made would have been motivated to modify the treatment method of Koya *et al.* by additionally providing an inhibitor of P-glycoprotein for the treatment of multi-drug resistant cancer and would have been imbued with at least a reasonable expectation that co-administering paclitaxel with a compound taught to improve the efficacy of paclitaxel in combination with an inhibitor of P-glycoprotein would improve the efficacy of paclitaxel in multi-drug resistant cancers. For example, if a cancer is known to be resistant to paclitaxel, the skilled artisan would have been motivated to co-administer a compound known to improve the anti-cancer activity of paclitaxel, such as Compound (1) in Koya et al., and would further be motivated to provide an inhibitor of P-glycoprotein in order to facilitate the treatment of the multi-drug resistant cancer, since it was known in the art as evidenced by Everitt et al. that inhibition of P-glycoprotein increases paclitaxel's potency, even in cells that show resistance to treatment with paclitaxel alone.

Accordingly, the instant claims are unpatentable over Koya et al. in view of Everitt et al. who teach, suggest, and motivate one skilled in the art to treat the claimed cancers with compositions comprising paclitaxel, a compound of the formula recited in the instant claims, and lopinavir, an inhibitor of P-glycoprotein.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejection of claims 8-14, 16-17, 25-31, 33-35, 37, 39, 43, 46-47, and 50 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 24-29 and 32-34 of U.S. Patent No. 7,385,084 is **withdrawn** in light of Applicant's filing of a Terminal Disclaimer.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614